UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/997,559	11/15/2001	David Botstein	P2730P1C40	5102

35489 7590 03/28/2006

HELLER EHRMAN LLP
275 MIDDLEFIELD ROAD
MENLO PARK, CA 94025-3506

EXAMINER	
DEBERRY, REGINA M	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 03/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/997,559	BOTSTEIN ET AL.	
	Examiner	Art Unit	
	Regina M. DeBerry	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 January 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *119-126 and 129-131* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *119-126 and 129-131* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Status of Application, Amendments and/or Claims

The amendment filed 09 January 2006 has been entered in full. Claims 1-118, 127 and 128 are cancelled. Claims 119-126 and 129-131 are pending and under examination. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 101 and 112, First Paragraph, Enablement

Claims 119-126 and 129-131 remain rejected under 35 U.S.C. § 101 because the claimed invention is not supported by a specific and substantial asserted utility or a well established utility. The basis for these rejections is set forth at pages 2-6 of the previous Office Action (14 October 2005).

Applicant reiterates that Table 9C of the instant specification indicates that PRO1187 showed a 2.25-fold to 2.928 fold amplification in squamous cell carcinoma of the lung. Applicant reiterates the Goddard Declaration and contends that a 2-fold increase in gene copy number in a tissue sample relative to a normal sample is significant and useful as a tumor marker. Applicant argues that they have submitted ample evidence from the art to show that, in general, if a gene is amplified in cancer, it is more likely than not that the encoded protein will also be expressed at an elevated level. Applicant discusses Orntoft *et al.,* Hyman *et al.* and Pollack *et al.* (references submitted by Applicant in a previous Office Action). Applicant reiterates the Polakis Declaration and contends that in general, there is a correlation between mRNA levels and polypeptide levels. Applicant contends that Hu *et al.* (reference submitted by the

Examiner in the previous Office Action) does not conclusively establish a prima facie case for lack of utility for the PRO1187 molecule. Applicant argues that the title of Hu *et al.,* "Analysis of Genomic and Proteomic Data Using Advanced Literature Mining", suggests that the conclusions in this reference are based upon statistical analysis of information obtained from published literature and not from experimental data. Applicant asserts that the conclusion of Hu *et al.* applies only to a specific type of breast tumor and cannot be generalized to breast cancer genes or cancer genes in general. Applicant criticizes the analytical methods utilized by Hu *et al.* Applicant maintains that when the proper legal stand is used, a prima facie case of lack of utility has not been met based on the references cited by the Examiner.

Applicant's arguments have been fully considered but are not deemed persuasive. The Examiner has discussed the references and declarations submitted by Applicant in the previous Office Action. The arguments are not deemed persuasive for reasons of record. The state of art regarding gene amplification and increase protein levels can be opposing as indicated by the references submitted by Applicant and the Examiner. Thus given the state of relevant art, the skilled artisan would not assume a correlation between gene amplification and protein levels. The skilled artisan would perform experiments to verify it. The instant examples *do not teach* increased PRO1187 mRNA or protein levels in squamous cell carcinomas of the lung. No mutation or translocation of PRO1187 has been associated with any type of cancer versus normal tissue. It is not known whether PRO1187 is expressed in corresponding normal tissues, and what the relative levels of expression are. In the absence of any of

the above information, all the specification does is present evidence that PRO1187 DNA is amplified in squamous cell carcinomas of the lung and invites the artisan to determine the significance of this increase. Increased copy number of DNA does not provide a readily apparent use for the polypeptide, for which there is no information regarding level of expression, activity or role in cancer. The scientific reasoning and evidence as a whole indicates that the rejection should be maintained.

Claims 119-126 and 129-131 remain rejected under 35 U.S.C. § 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art would clearly not know how to use the claimed invention. The basis for these rejections is set forth at pages 2-6 of the previous Office Action (14 October 2005). Applicant incorporates their response to the rejection under 35 USC 101 in response to the rejection under 35 USC 112, first paragraph. Applicant's arguments have been fully considered but are not found to be persuasive for reasons of record and the reasons discussed above in the maintained 35 USC 101 rejection.

Claim Rejections - 35 USC § 112, First Paragraph, Written Description

Claims 119-123 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed,

had possession of the claimed invention. The specification provides adequate written description for SEQ ID NO:399, but not variants. The basis for these rejections is set forth at pages 6-8 of the previous Office Action (14 October 2005).

Applicant discusses the legal test for written description and various case law. Applicant argues that the specification provides ample written support for determining percent sequence identity between two amino acid sequences and the specification provides detailed guidance as to the changes that may be made to a PRO polypeptide without adversely affecting its activity. Applicant cites various pages in the specification. Applicant states that pending claims 119-123 recite the functional limitation that the nucleic acid encoding said polypeptide is amplified in squamous cell carcinomas of lung. Applicant argues that the specification provides written support for detecting and quantifying amplification of such nucleic acids in several tumors and/or cell lines as described in Example 170. Applicant cites Enzo Biochem., Inc. v. Genprobe, Inc. 296 F.3d 1316 (Feb. Cir. 2002) and the USPTO's Written Description Examination Guidelines. Applicant argues that the instant claims meet the standard set by the Enzo court in that the claimed sequences are defined not only by functional properties, but also by structural limitations.

Applicant's arguments have been fully considered but are not found to be persuasive. Applicant cites pages in the specification but there is no description of variants of SEQ ID NO:399 that exist, while still maintaining function. Specific, not general guidance is what is needed. The instant specification contemplates but does not exemplify variants of the protein wherein the variant can have any number of

substitutions, deletions, insertions and/or additions in SEQ ID NO:399, wherein said nucleic acid encoding said polypeptide is overexpressed in squamous cell carcinomas of lung. Applicant cites Example 170 (Gene Amplification in Tumors) but the instant example does not provide any guidance as to what changes should be made and which regions of the instant protein are functionally and structurally critical. There is no description of variants of SEQ ID NO:399 that exist, while still maintaining function. The Enzo case law and Written Description Guidelines are not applicable to the instant claims. The only factors present in the claims are a partial structure in the form of a recitation of percent identity, a requirement that the sequence be native, and a requirement that the encoding nucleic acids are amplified in lung tumors. There is no identification of any particular portion of the structure that must be conserved in order to conserve the required function. There are no structural attributes or features that are common to members of the genus. Furthermore, the term "native sequence" encompasses naturally-occurring truncated or secreted forms, naturally-occurring variant forms and naturally-occurring allelic variants of the PRO polypeptide. None of these sequences meet the written description provision of 35 USC 112, first paragraph. The courts have specifically stated that the skilled artisan cannot envision the *detailed chemical structure* of an encompassed polypeptide until the structure is disclosed, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25

USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016. In the instant case, SEQ ID NO:399 has been disclosed, but no native sequence variants thereof have been disclosed regardless of whether or not they are encoded by nucleic acids that are amplified in lung tumors. Additionally, there is the issue of whether or not the single disclosed embodiment is actually amplified in lung tumors (see maintained rejections under 35 U.S.C. §§ 101 and 112, first paragraph, above). Clearly, such does not constitute disclosure of a representative number of examples of, nor adequate written description for, the claimed genus. The scientific reasoning and evidence as a whole indicates that the rejection should be maintained.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Regina M. DeBerry whose telephone number is (571) 272-0882. The examiner can normally be reached on 9:00 a.m.-6:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda G. Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

RMD
3/21/06

Marianne P. Allen
MARIANNE P. ALLEN
PRIMARY EXAMINER
3/23/06
AU1647